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Macronutrient Intake in Preschoolers with Cystic Fibrosis and the Relationship between Macronutrients and Growth

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Abstract

Background—Adequate nutrition is essential for growth in children with cystic fibrosis (CF). The new CF Foundation Clinical Practice Guidelines bring attention to monitoring macronutrient intake as well as total energy.

Methods—Dietary intake of 75 preschool children with CF and pancreatic insufficiency was examined and compared to the Clinical Practice Guidelines. Regression analyses examined relationships between macronutrient intake and growth.

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Results—Approximately 45% of children met the 110% minimum recommended dietary allowance (RDA) recommendation. Children consumed 35.3% (6.1) of total daily energy intake from fat, 12.7% (1.7) from protein, and 52.0% (6.1) from carbohydrate. Percent energy from protein was associated with height growth.

Conclusions—Many preschoolers with CF are not meeting nutrition benchmarks for total energy and fat. To optimize nutrition early, dietary monitoring with frequent individualized feedback is needed. Optimizing intake of macronutrients that promote growth, especially fat and protein, should be a primary clinical target.

List of Key Words

children; nutrition; behavioral intervention

INTRODUCTION

To optimize diet, adequate intake of all macronutrients is essential in healthy populations [1], and may even be more important in populations with chronic illness, such as in children with cystic fibrosis (CF). In general the goal for children with CF is to achieve optimal growth [2, 3] by consuming a daily energy (kcal) intake of 110–200% of the recommended daily allowance (RDA) [2, 4, 5] with at least 35–40% of daily energy derived from fat [3]. Studies investigating macronutrient intake other than fat in children with CF are limited. Until the recent Clinical Practice Guidelines from the CF Foundation for preschoolers were published [6], dietary goals for protein intake received little attention particularly for preschool-aged children. The Clinical Practice Guidelines are the first ever published specifically for preschool-aged children with CF, and there is a specific recommendation for protein, that 2–3 year-olds consume at least 13 grams of protein per day and 4–5 year olds consume at least 19 grams of protein per day [1, 6] which are based on the recommendation for the general population.

In CF better nutritional status early in life is associated with improved clinical and survival outcomes, but the extent to which preschool children are meeting these new guidelines is unknown [7–9]. In particular, achieving adequate protein intake in children with CF may be essential due to loss of muscle mass [10], which may not be counteracted by solely focusing on energy intake from any macronutrient source [11, 12]. Protein intake is essential for building and restoring the body to promote growth, which is interrelated with pulmonary function [13–15], and plays a role in endocrine and immune functioning, in addition to providing energy and glucose as needed [16].

In light of the recently published guidelines, this paper describes the dietary intake of the largest-available sample of preschoolers with CF with dietary intake information. Dietary data were analyzed from a large multisite randomized clinical trial (RCT) of preschool-aged children with CF examining the effectiveness of a behavioral and nutrition treatment (BEH) compared to an education and attention control treatment (CONTROL) to improve intake and growth [17]. Specific aims of the current study were to describe the baseline dietary intake of preschoolers, including percentage of children reaching recommended benchmarks and the distribution of macronutrient intake overall and by meal. We also examined the

relationship of macronutrient intake to growth. The goal of the BEH in the RCT was to increase daily energy intake, however no specific macronutrient goals were set within the intervention. We anticipated that fat and protein would increase as daily intake increased, and that fat and protein intake would demonstrate a relationship with growth.

METHODS

Participants

Children were part of a larger RCT that compared BEH to CONTROL in children aged 2 to 6 years diagnosed with CF and pancreatic insufficiency (PI) to increase daily energy intake and growth [17]. Children were enrolled in the RCT at seven accredited CF Centers in the United States. The study was approved by the Institutional Review Board at each site, and families provided written informed consent. Inclusion criteria included confirmed diagnosis of CF based upon meeting two of the following criteria: sweat chloride by quantitative pilocarpine electrophoresis ≥ 60 mEq/L; two clinical features consistent with CF; or genetic testing demonstrating mutations associated with CF; confirmation of PI (based on fecal elastase of < 100 micrograms per gram of stool (Kaleida Health Women and Children's Hospital Laboratory, Buffalo, New York); at least 6 months post CF diagnosis; and no restrictions in consuming a high fat diet. Exclusion criteria included baseline weight for age (WAZ) z score > 1.0 (age and sex adjusted) determined by the Centers for Disease Control and Prevention (CDC) Anthropometric Software Program (2000 data, Division of Nutrition, CDC); current use of supplemental nutrition through enteral or parenteral feeding; diagnosis of other conditions or use of current medication known to affect growth; diagnosis of developmental delay; genetic potential for height as acceptable according to the 2001 Consensus Conference guidelines [3] and dietary intake exceeding 140% of the average estimated energy requirement (RDA; based on sex, age, and physical activity level) [1].

A total of 163 children were assessed for eligibility and 78 were randomized into the original trial. Among the 78 randomized, 75 had at least 3 dietary records at the baseline assessment and were included in this analysis.

Measures

Participant demographics were collected via a parent-completed questionnaire at baseline only. All anthropometric and dietary measures were taken at baseline and post-treatment (6-months).

Anthropometrics—Weight and height were measured by an expert in anthropometry using standard procedures and blinded to the child's treatment group assignment. The child's weight in kilograms, measured to the nearest 100 grams was obtained using a digital scale (Scaletronix Inc.). The child's height was measured to the nearest millimeter using a stadiometer (Holtain). Height was obtained standing unless the child was unwilling to stand then the supine measurement was obtained. All measures were obtained in triplicate with the mean used for analyses. WAZ and height-for-age z-scores (HAZ) were standardized relative to the population mean and standard deviation for the child's age and sex according to the

CDC [18]. Body mass index (BMI) percentile was also determined according to 2000 CDC age and sex-specific growth charts [18].

Dietary Intake—Dietary intake of each child was assessed using a seven-day dietary record completed by parents. Within the larger trial, parents were taught how to measure food and to record information on the food records after each snack and meal. In unique situations when a family was unable to consistently record the child's daily intake, a Registered Dietitian (RD) contacted the family by phone to collect the information through three 24-hour food recalls (two weekdays and 1 weekend day).

All dietary records were reviewed for completeness and accuracy by a RD. Dietary data were entered into Nutrition Data System for Research (NDSR) software (developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis MN) by a blinded, independent research RD and analyzed for average daily energy intake, percent energy from carbohydrate, percent energy from protein, percent energy from fat, and grams of protein.

Statistical Analysis

Descriptive statistics were calculated for average daily energy intake, average percent energy from each macronutrient (carbohydrate, protein, fat), grams of protein intake, average percent RDA, and kcal/kg. Continuous variables were summarized using means and standard deviations, and categorical variables were summarized using frequencies and percentages. We examined correlations between macronutrient intake using Pearson's correlation coefficient (r). Energy intake and macronutrient variables were further examined by age and by meal (breakfast, lunch, dinner, snack). If two of the same meal type (i.e., two recorded breakfasts on one day) were reported within a day each energy and macronutrient intake variable was averaged. For snacks, energy and macronutrient intake were summed across the day if multiple snacks were consumed within one day. Baseline dietary intake was compared to recommended benchmarks to determine the number of children meeting recommendations.

While the focus of this investigation was to describe dietary intake of children prior to entering treatment, we also examined changes in intake over time by treatment condition to examine associations with growth. To analyze changes in macronutrient intake over time a linear mixed model, controlling for child age, was used to analyze the main effects of time (baseline, post-treatment), treatment (BEH, CONTROL) and a time-by-treatment interaction effect for percent energy from each macronutrient. The relationships between percent energy from macronutrient intake (percent energy from carbohydrate, percent energy from protein, percent energy from fat) and growth (HAZ, WAZ) were examined using similar linear mixed effects models controlling for child age. Each model included subject-specific random intercepts to account for longitudinal correlation and between-subject heterogeneity. To account for missing data, effects in linear mixed effects models were estimated using all available data and maximum likelihood [19]. Results from each model are expressed as the F-statistic from the corresponding Type III test of fixed effects. P-values < 0.05 were considered statistically significant. All analyses were conducted in SAS (version 9.3, SAS Institute®, Cary, NC).

RESULTS

Of the 75 children included in this analysis, the mean age was 3.8 (1.3) years with a baseline WAZ of -0.41 (0.80), HAZ of -0.51 (0.81), and 44% had a BMI less than the 50th percentile. Given there were no significant differences between groups on dietary intake prior to treatment, other than the BEH group consumed significantly more percent energy from carbohydrate ($p=0.04$), intake for both treatment groups was collapsed in order to examine descriptive statistics regarding overall dietary intake for the entire sample.

Total energy and macronutrient intake

At baseline mean daily energy intake was 1462 (329) kcal/day with an average of 35.3% (6.1) of daily percent energy intake from fat, 12.7% (1.7) from protein, and 52.0% (6.1) from carbohydrates. On average children were consuming 45.9g (12.1) of protein per day. Total energy intake and percent energy intake from macronutrients was also examined by age (Table 1). There was a strong negative correlation at baseline between carbohydrate and fat intake, $r = -0.97$, $p < 0.001$, indicating the more percent carbohydrates consumed the less relative fat percent consumed. When energy intake and macronutrient intake were examined by age, energy intake increased with age as expected, but percent energy from macronutrients did not differ by age.

Achievement of intake (total energy and macronutrient) and growth benchmarks

For comparisons to recommended benchmarks the average RDA achieved at baseline was 109.5% (25.8) with only 45% of all children meeting the 110% minimum RDA recommendation. Only 53% of children were meeting the minimum 35% daily energy from fat recommendation. Notably, all of the children were meeting the protein recommendation.

Of the 44% of children in the sample defined at nutritional risk ($< 50^{\text{th}}$ BMI percentile), 55% were not meeting the 110% minimum RDA and only the 2 and 4 year olds in this nutritional risk category were meeting the 110% RDA. Children meeting the optimal nutritional threshold (50^{th} BMI percentile) were consuming an average of 94 kcal/kg per day, within the 90–110 kcal/kg per day recommendation to sustain growth [6]. (Table 1).

Macronutrient intake by meal

Average percent energy from macronutrients was also examined by meals and snack (Table 2). Dinner was the meal with the highest consumed percent energy from fat, with lunch also a notable contributor to fat intake. Lunch and dinner were the meals with the highest percent protein intake. Relative to meals, snack had the highest percent energy from carbohydrate and was lower in percent energy from protein.

Macronutrient intake over time

Percent energy from fat significantly increased from baseline and post-treatment ($p=0.02$) with a non-significant treatment by time interaction ($p=0.08$). Percent energy from protein decreased from baseline to post-treatment regardless of treatment group, and while this decrease was statistically significant ($p < 0.01$) the amount of change was a difference of 1%

(SE=0.24) and reflected stability more than clinically significant change. Change in percent energy from carbohydrate from baseline to post-treatment was non-significant.

Macronutrient intake and growth

In terms of growth, change in percent energy from protein was a significant predictor of change in HAZ from baseline to post-treatment, $F(1,125)=12.93$, $p<0.001$ for the combined sample. While change in percent energy from protein was not a significant predictor of change in WAZ over time, there was a trend towards significance, $F(1,127)=3.06$, $p=0.08$. Change in percent energy from fat or carbohydrates did not significantly impact change in HAZ or WAZ.

DISCUSSION

This study represents a contemporary sample of preschoolers receiving standard of care nutrition at their respective accredited CF Centers in the US. The increased focus on improving the nutritional status in patients with CF over the last 10 years has contributed to more children receiving proactive assessment and intervention, and achieving daily intake that often resembles the intake of peers without CF. While this is an impressive achievement, many children are not consuming sufficient energy to promote optimal growth.

Upon entering the trial, the percent RDA for the children in the trial was similar to that seen in previously published studies [20, 21], and more than half (55%) of the preschoolers were not meeting the minimum 110% RDA for energy recommendation, and 44% of children had BMIs <50th percentile. The average daily percent energy from fat consumed for the entire sample was just at the minimum recommendation of 35%, and only 53% of the children were meeting this recommendation, suggesting some children were higher consumers of fat and other children were in need of nutritional tracking and intervention in this key area. Children were within the acceptable macronutrient distribution range (AMDR) for carbohydrates and protein.

Establishing an approach to feeding during the preschool years that involves systematic monitoring, goal setting, and timely feedback about nutrition intake can help parents of children with CF to engage in feeding practices that set the stage for achieving optimal nutrition outcomes. Behavior-nutrition treatments [17, 20] have demonstrated that this approach can increase energy intake and have a positive impact on growth. To date, traditional clinical and research interventions have targeted increasing energy intake broadly however and have not set macronutrient goals specifically.

Assessing daily energy intake to inform recommendations for increasing intake in children with CF is essential when growth is not meeting recommended benchmarks. One approach to boosting total daily energy intake is providing basic recommendations about routine ways to increase overall energy intake, and may rely on diet tracking and monitoring to guide recommendations or progress with achieving recommendations. In order to guide and refine nutrition interventions, these data emphasize the need to more consistently use dietary tracking tools (e.g. MyFitnessPal™) to allow for investigation of dietary data beyond total energy intake. Tracking informs the identification of specific targets, allows for more

targeted and individualized recommendations to be provided, and the ability to monitor progress toward these targets carefully. Such targets could include boosting calories for a particular meal or snack or increasing the intake of a specific macronutrient. Moreover, even when children with CF are achieving growth benchmarks, specifically monitoring and targeting macronutrients such as fat or protein in addition to total energy may be necessary to promote optimal growth and health and improve diet quality.

Since most children eat in terms of meals and snacks, understanding the macronutrient intake at each eating occasion can better help families optimize their child's dietary intake over a day. Targeting a meal, such as breakfast, could be an important intervention, as less percent energy from fat and protein and more percent energy from carbohydrates were consumed at this meal, relative to other meals and snack. Breakfast provided the lowest percent energy from protein, but it was still within the AMDR for a non-CF population.

Snacking is a common eating behavior in preschool-aged children. On average the children in this study consumed about two snacks per day with 60% of energy coming from carbohydrates. While this is within the AMDR, children with CF will benefit from snacks with increased energy from protein and fat. Given there are multiple opportunities for snack each day, targeting snacks can optimize nutrition overall and increase fat intake during these eating opportunities. The inverse relationship found between fat and carbohydrate consumption at baseline highlights the dynamic relationship between macronutrients. Given that it may be more difficult to identify snacks that are both high in healthy fat and protein, specific recommendations for such combinations should be given to families. Without specific recommendations families are likely to default to offering foods and beverages high in carbohydrates, such as fruit and fruit juice, a preferred source at this stage of development [22] without including addables and spreadables that would increase calories from fat.

Notably, all children in the sample were meeting protein recommendations. While there was a decrease in protein during the 6-month time frame, the decrease was clinically negligible (approximately a 1% decrease) and there was limited variability in protein intake ($SE=0.24$). The high and stable protein intake likely contributed to the positive change in HAZ. Alternatively, an increase in percent energy consumed from fat (2% increase) was not associated with significant changes in HAZ or WAZ. There was much greater variability in percent energy consumed from fat ($SE=0.85$), and while fat intake increased somewhat, most of the children were not meeting minimum fat recommendations at baseline. Perhaps due to malabsorption from PI, further increases in consumption of fat are necessary to have a positive impact on growth even when enzyme dosing is optimized.

Findings suggest there may be a large threshold in regards to finding a relationship between macronutrient intake and growth. Additional research is certainly needed to address the complexity of what preschoolers with CF need to grow in accordance with recommendations, including more frequent sampling of nutrition intake to observe variability and patterns of intake to that affect growth. Notably, just over half (55%) of children at nutritional risk ($BMI < 50^{\text{th}}$ percentile) were consuming less than the 110% RDA at baseline. All of the children with a $BMI > 50^{\text{th}}$ percentile had daily intake meeting the new 90–110 kcal/kg per day recommendation but 55% of these children were consuming less

than the 110% RDA. Therefore, some preschoolers may be able to achieve adequate growth without achieving the 110% RDA.

The results of this study combined with the Clinical Practice Guidelines [6] indicate that the macronutrients contributing to energy intake may be important in preschool children with CF, particularly in relationship to growth. With few trials conducted in preschool-aged children with CF these findings offer important information for future research and clinical practice, yet need to be interpreted within the context of the limitations. The study's sample size and the trial's inclusion criteria allowing children with a WAZ up to 1.0 may have limited findings related to change in WAZ. While the use of self-reported dietary measures can be a limitation, all children included in the study completed at least three weighed dietary records and most completed seven weighed dietary records providing a more precise estimate of consumption [23].

Conclusion

Many preschool children are not meeting CF nutrition and growth recommendations. A combined nutrition-behavioral intervention is recommended for children with CF who are not meeting growth benchmarks. Interventions to increase nutrition intake could be further refined by including tracking and monitoring of macronutrients in addition to total energy. Increasing intake of macronutrients that have a greater impact on energy intake and growth should be a primary clinical target.

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Additional Contributions:

Additional Information: For more information regarding this trial, please visit: <http://www.cincinnatichildrens.org/research/divisions/b/psychology/labs/powers/>

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Highlights

- At baseline mean daily energy intake was 1462 (329) kcal/day with an average of 35.3% (6.1) of daily percent energy intake from fat, 12.7% (1.7) from protein, and 52.0% (6.1) from carbohydrates.
- The average RDA achieved at baseline was 109.5% (25.8) with only 45% of all children meeting the 110% minimum RDA recommendation.
- Only 53% of children were meeting the minimum 35% daily energy from fat recommendation.
- All of the children were meeting the protein recommendation.
- Change in percent energy from protein was a significant predictor of change in HAZ from baseline to post-treatment for the combined sample.

Table 1 Baseline Dietary Characteristics by Age. Shown as mean (standard deviation) and p values indicate significance difference between age.

	Overall (n = 75)	2 years (n = 26)	3 years (n = 21)	4 years (n = 11)	5 years (n = 14)	6 years (n = 3)	p-value
Daily total energy (kcal) intake	1462 (329)	1344 (281)	1355 (336)	1539 (272)	1686 (218)	1899 (476)	0.0006
% kcal from fat	35.3 (6.1)	35.3 (6.8)	36.9 (5.4)	34.9 (4.7)	34.5 (6.4)	31.3 (7.7)	0.5545
% kcal from protein	12.7 (1.7)	12.2 (1.4)	12.6 (2.3)	12.9 (1.3)	13.2 (1.4)	13.6 (0.8)	0.3632
% kcal from carbohydrate	52.0 (6.1)	52.6 (6.8)	50.5 (5.8)	52.2 (4.6)	52.3 (6.2)	55.2 (8.6)	0.6865
% of RDA	110 (26.0)	128 (26.1)	94 (22.9)	102 (19.2)	105 (12.8)	116 (29.0)	<0.0001
<50 th percentile for BMI	110 (16)	120 (20)	102 (15)	114 (12)	106 (9)	99 (10)	0.0976
50 th percentile for BMI	109 (31)	132 (29)	86 (27)	97 (20)	105 (17)	148 (-)	0.0005
Kcal/kg							
<50 th percentile for BMI	105 (16)	110 (18)	105 (17)	110 (13)	103 (13)	86 (8)	0.4631
50 th percentile for BMI	94 (25)	108 (25)	80 (23)	89 (22)	86 (11)	127 (-)	0.0176

Table 2

Baseline Total Energy and Percent Energy from Macronutrients at Meals and Snack. Shown as mean (standard deviation).

Baseline (n = 75)	
Breakfast	
Total kcal	337.0 (162.1)
% kcal from fat	31.3 (14.4)
% kcal from protein	11.6 (4.9)
% kcal from carbohydrates	56.7 (16.8)
Lunch	
Total kcal	361.4 (197.0)
% kcal from fat	38.3 (13.5)
% kcal from protein	14.3 (5.9)
% kcal from carbohydrates	47.4 (15.5)
Dinner	
Total kcal	394.4 (200.9)
% kcal from fat	38.6 (13.2)
% kcal from protein	15.6 (6.8)
% kcal from carbohydrates	45.9 (15.6)
Snack	
Total kcal	216.9 (148.3)
% kcal from fat	30.0 (15.7)
% kcal from protein	8.8 (5.5)
% kcal from carbohydrates	64.3 (19.0)

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